UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,544	12/18/2000	Mark B. Pepys	P 0275486 / 201045/JND	1521

909 7590 09/02/2005

PILLSBURY WINTHROP SHAW PITTMAN, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,544	PEPYS, MARK B.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 42-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 42-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of invention group I, claims 1-25, and 42-56, directed to method of using phosphorycholine or its derivative for treating tissue damage and inflammatory associated disorders, in the reply filed on June 15, 2005 is acknowledged.

Claim Rejections 35 U.S.C. 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating atherosclerosis (see pages 20-37 of the specification herein), does not reasonably provide enablement for preventing atherosclerosis, and for treating and/or preventing of tissue damage in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

4. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. The court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The claims are directed to treating and/or preventing tissue damage. "tissue damaging" herein essentially reads on all disorders, including, atherosclerosis, cancers, Alzheimer's disease, viral infections. The state of the art in treating such diseases is low. There is no established method for preventing such disease in the art. It is known it the art that excess amounts of human CRP would induce myocardial infarction, markedly increases morbidity, mortality and the infarct size in animal model (Griselli et al.). Applicant provides evidence showing that, in the same model, CRP inhibitor would suppress the pathogenic effect of CRP. (pages 20-35 herein). The specification provide no further guidance, direction or working examples as how the claimed method would be effective in preventing atherosclerosis, no does it provide guidance, direction or working examples for treating and preventing other tissue damage. The underline etiology of atherosclerosis, as well as other diseases associated with tissue damaging (cancers, Alzheimer, etc), are complex and unclear. The art and the instant application have shown that excess amount of CRP may cause tissue damage. However, there is no evidences that CRP is solely response for causing tissue damage. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. The instant claims read on preventing and/treating preventing and/treating all diseases associated with tissue damage, necessitating an

exhaustive search for the embodiments suitable to practice the claimed invention, absent undue experimentation.

Claim Rejections 35 U.S.C.§ 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim Rejections 35 U.S.C.§ 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-25 and 42-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhakdi et al. (IDS) and Kito, in further view of Yedgar et al. (US 5,064,817) and Wissner et al. (US 4,640,913).

4. Bhakdi et al. and Kito teaches that phosphorylcholine are useful for inhibiting the binding of CRP to LDL, wherein the binding of CRP to LDL is known to be a factor of atherosclerosis. See the abstracts.

5. The primary references do not teach expressly the employment of hexadecyl phosphorylcholine for treating atherosclerosis.

6. However, Yedgar et al. teaches that various phosphorylcholine derivatives are known to be useful for treating pathological conditions including atherosclerosis. See, particularly, column 13, lines 22-38, and the claims. Wissner et al. teaches various phosphorylcholine derivatives are useful for treating hypertension, an underline etiology of atherosclerosis. See, particularly, the abstract, column 1, lines 19-26, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis.

A person of ordinary skill in the art would have been motivated to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis because phosphorylcholine is known to inhibiting the binding of CRP to LDL is known to be a factor of atherosclerosis, suggesting the usefulness of phosphorylcholine for treating atherosclerosis, and a ester, or salt of an active therapeutical compound, would have considered, an equivalent of the active therapeutical compound. Further, phosphorylcholine derivatives are generally known to be useful for treating atherosclerosis. With respect to stroke, note, a method known to be useful for treating the underline etiology of a disorder would have been reasonably expected to be useful for treating or preventing the disorder.

7. Claims 1-25 and 42-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhakdi et al. (IDS) and Griselli et al. (IDS) in further view of Yedgar et al. (US 5,064,817) and Wissner et al. (US 4,640,913).

8. Bhakdi et al. teaches that phosphorylcholine are useful for inhibiting the binding of CRP to LDL, wherein the binding of CRP to LDL is known to be a factor of atherosclerosis. See the

abstracts. Griselli et al. teaches that excess amounts of human CRP would induce myocardial infarction, markedly increases morbidity, mortality and the infarct size in animal model (Griselli et al.)

9. The primary references do not teach expressly the employment of hexadecyl phosphorylcholine or phsphorylcholine for treating atherosclerosis.

10. However, Yedgar et al. teaches that various phosphorylcholine derivatives are known to be useful for treating pathological conditions including atherosclerosis. See, particularly, column 13, lines 22-38, and the claims. Wissner et al. teaches various phosphorylcholine derivatives are useful for treating hypertension, an underline etiology of atherosclerosis. See, particularly, the abstract, column 1, lines 19-26, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis.

A person of ordinary skill in the art would have been motivated to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis because it is known that excessive amount of CRP would cause atherosclerosis lesion, and phosphorylcholine is known to inhibiting the binding of CRP to LDL, which is known to be a factor of atherosclerosis, suggesting the usefulness of phosphorylcholine for treating atherosclerosis. Further, an ester, or salt of an active therapeutical compound, would have considered, an equivalent of the active therapeutical compound. Furthermore, phosphorylcholine derivatives are generally known to be useful for treating atherosclerosis. Withr respect to stroke,

note, a method known to be useful for treating the underline etiology of a disorder would have been reasonably expected to be useful for treating or preventing the disorder.

11. Claims 1-25 and 42-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeh et al. (US 6,764,826) in view of Bhakdi et al. (IDS), and in further view of Yedgar et al. (US 5,064,817) and Wissner et al. (US 4,640,913).

12. Yeh et al. teaches a method of treating inflammatory related diseases by inhibiting C-reactive protein, wherein the diseases including atherosclerosis, ischemic heart disease, cardiovascular complication, etc. See, particularly, column 3, line 59 to column 4, lines 25. Yeh et al. further reveals that excessive amount of C-reactive protein is a known risk factor for atherosclerosis, and other cardiovascular disorders. See, particularly, columns 1-2.

13. The primary references do not teach expressly the employment of hexadecyl phosphorylcholine or phosphorylcholine for treating atherosclerosis.

14. However, Bhakdi et al. teaches that phosphorylcholine are useful for inhibiting the binding activity of CRP. See the abstracts. Further, Yedgar et al. teaches that various phosphorylcholine derivatives are known to be useful for treating pathological conditions including atherosclerosis. See, particularly, column 13, lines 22-38, and the claims. Wissner et al. teaches various phosphorylcholine derivatives are useful for treating hypertension, an underline etiology of atherosclerosis. See, particularly, the abstract, column 1, lines 19-26, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis or other cardiovascular diseases.

A person of ordinary skill in the art would have been motivated to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis, or other cardiovascular diseases because phosphorylcholine is a known inhibitor of CRP. Further, it is generally known that excessive amount of CRP would be a risk factor for atherosclerosis. Further, an ester, or salt of an active therapeutical compound, would have considered, an equivalent of the active therapeutical compound. Furthermore, phosphorylcholine derivatives are generally known to be useful for treating atherosclerosis. Withr respect to stroke, note, a method known to be useful for treating the underline etiology of a disorder would have been reasonably expected to be useful for treating or preventing the disorder.

Response to the Arguments

Applicants' amendments and remarks submitted November 29, 2004 have been fully considered, but are found unpersuasive.

Applicants argues that, contrary to the teaching by the cited references (Bhakdi et al. in particular), at the time the claimed invention was made, persons of ordinary skill in the art only recognized that physiological activity of CRP in inflammatory and tissue damaging conditions was not understood and could not be predicted. Applicants particularly argues that, at the time the claimed invention was made, "CRP was known to augment complement activation at the site of tissue injury;" but "CRP was also known to protect the tissues from assembly of terminal complement components" Applicants also cites a recent publication by Bhakdi et al. which shows possible protective role of CRP in atherogenesis. Applicant's arguments are unpersuasive.

Initially, it is noted that the claimed invention has been rejected as it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made. Therefore,

the recent publication of Bhakdi et al is moot to the rejection. Further, the recent publication by Bhakdi et al. is by no mean "a retraction of the hypothetical proposal stated in the Bhakdi et al.(1999)" the works of Bhakdi et al. as well as other publications about CRP, merely shows two aspects of CRP, at normal level, and at a level with elevated amount of CRP. See, page 1874 in Bhakdi et al (2004). Bhakdi et al. clearly indicate the usefulness of inhibiting CRP activities for reducing the development of atherosclerosis. Attention is further directed to columns 1-2 in Yeh et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617